degeneration under excessive mechanical loads and potential AF repair or regeneration using adequate mechanical stimulation.
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MATRIX ELASTICITY-DEPENDENT DIFFERENTIATION OF ANNULUS FIBROUS-DERIVED STEM CELLS

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Background: Annulus fibrosus (AF) injuries commonly lead to substantial intervertebral disc (IVD) degeneration, the major cause of lower back pain which affects about 80% of the population. Recently, tissue engineering has evolved into a promising approach for AF regeneration. While a lot of attempts have been made during the last decade, constructing engineered AFs remains challenging due to the tremendous complexity of AF tissue at cellular, biochemical, microstructural, and biomechanical levels. It is known that the elasticity of matrix effectively directs the lineage specification of stem cells.
Methods: We synthesized a series of biodegradable poly(ether carbonate urethane)urea (PECUU) materials whose elasticity approximated that of native AF tissue. Fibrous PECUU scaffolds were fabricated by electrospinning technique and used for culturing AF-derived stem cells (AFSCs). The growth, gene expression, biochemical and biomechanical characteristics of AFSCs were studied. In particular, we explored the potential of AFSCs to achieve diversified differentiation of cells by varying the elasticity of substrate.
Results: By adjusting the molecular weight of polycarbonates, ratios of hard segment to soft segment, a series of polyurethanes were obtained with different elastic modulus (PECUU1, 13.4MPa; PECUU2, 6.4MPa; PECUU3, 5.1MPa; PECUU4, 2.5MPa), which is close to the elastic modulus of AF tissue. When AFSCs were cultured on electrospun PECUU fibrous scaffolds, the gene expression of collagen-I in them increased with the elasticity of scaffold material, whereas the expression of collagen-II and aggrecan genes showed an opposite trend. At protein level, the content of collagen-I gradually increased with substrate elasticity, while collagen-II and GAG contents decreased. In addition, the cell traction forces (CTFs) of AFSCs gradually decreased with scaffold elasticity. Such substrate elasticity-dependent changes of AFSCs were similar to the gradual transition in the gene, biochemical, and biomechanical characteristics of cells from inner to outer regions of native AF tissue.
Discussion and Conclusion: Together, findings from this study have, for the first time, implied that depending on the substrate elasticity, AFSCs may differentiate into various types of AF-like cells. Therefore, this study provides solid basis for the use of AFSCs, along with scaffolds of varying elasticity, for AF tissue engineering.
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HOW PATIENT-OPTIMISED DEVICE CONFIGURATION CAN PROVIDE FRACTURE SITE STIMULATION AND REDUCE AGE-RELATED SCREW LOOSENING RISK IN LOCKED PLATING

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Objective: When using locked plating for bone fracture fixation, screw loosening is reported as one of the most frequent complications and is commonly attributed to an incorrect choice of screw configuration. Choosing a patient-optimised screw configuration is not straightforward as there are many interdependent variables that affect device performance. The aim of the study was to develop a framework for device selection and configuration based on three key variables of interest: (1) interfragmentary motion (IFM); (2) strain concentrations around screws; and (3) stress levels within the plate.
Methods: Finite element models of a tibia with a comminuted diaphyseal fracture were developed incorporating cortical bone heterogeneity, orthotropy and geometrical nonlinearity. Strain concentrations around screws (SCS) were used as indicators of regions that may undergo loosening. Plate stress, SCS and IFM and were measured for a total of 10 different screw configurations and two different bone qualities (20 unique models). Axial and torsional load cases were considered.
Results: The study found that the material of the plate and the size of the bridging span influenced all three variables of interest. Screw spacing was found to be particularly influential in poorer bone quality. Leaving two empty holes between screws near the fracture reduced SCS by 49% in osteoporotic bone compared to 2.4% in healthy bone. Unlike bridging span, modifications to screw spacing had a negligible effect on IFM or plate stress levels. Under torsional loading, the importance of screw placement was similar for the two bone qualities.
Conclusion: Due to the large number of device variables and patient factors, the current guidelines regarding locking screw placement are somewhat unclear. This study provides valuable information regarding the configuration of locked plate devices for specific individuals. The results are presented in a decision making tree representing the first step towards comprehensive guidelines.
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STIFFNESS IN LIVING CARTILAGE INCREASES AFTER SELF-MATING ARTICULATION—A NANOINDENTATION STUDY

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Introduction: While studies have demonstrated that osteoarthritis is linked to the softening of articular cartilage, the effect of tribological stress on cartilage mechanical properties is not well-understood. Nanoindentation has made mechanical characterizations of biological tissues at micro- and nano-scales possible. However, using nanoindentation on cartilage is challenging due to its heterogeneous, biphasic, and soft material properties. In this study, we developed a method to characterize articular cartilage explants using the Ti-950 Triboindenter by Hysitron®. Once we established a repeatable nanoindentation method, we compared mechanical properties of live cartilage explants before and after undergoing self-mating articulation in a joint motion simulator.
Methods: Cartilage explants were obtained from the patella-femoral groove of 24-week-old bovine and placed in DMEM/F12 media at 37°C. For method development, phosphate buffered saline was added to keep freeze-thawed explants hydrated during indentation with a 20um-indenter in order to optimize parameters including fluid levels and software settings. To test for reproducibility, we performed duplicates of five indents in five regions on the explant. A joint simulator that applies complex motion patterns on explants was utilized. Load (40N) and shear were applied to live explants for 3 hours (5400 cycles) using a modified hip-ball onto which a live cartilage strip is sutured, creating a cartilage-on-cartilage (CoC) interface with the explant. We performed a 3X3 array of 8um deep indents in the articulated and non-articulated regions of the explant before and after articulation ($n=18$ indents). In one explant, nanoindentation was performed one hour and three hours post-articulation to observe potential changes in mechanical properties over time ($n=9$ indents).
Results: In method development, we found that factors including fluid level and indent setpoint influence the Young's Modulus (E). For reproducibility, we used a paired t-test analysis and found no significant differences between duplicates ($E=367\pm7$kPa, $p=0.809$). For our pre- and post-CoC articulation stiffness comparisons, a one-way ANOVA analysis blocked by animal demonstrated that following articulation, E significantly increases in the articulated region ($p<0.001$) but not in the surrounding unworn region ($p=0.26$). In the non-articulated region, $E_{pre\text{-}test}=124\pm8$kPa and $E_{post\text{-}test}=137\pm8$kPa, whereas in the articulated region, $E_{pre\text{-}test}=105\pm30$kPa and $E_{post\text{-}test}=461\pm30$kPa. Additionally, 3hr-post-articulation indentation results indicated that in the articulated region, $E=127\pm5$kPa, demonstrating that with time, articular cartilage stiffness may return to its pre-articulation conditions.
Discussion and Conclusion: We found that the stiffness of live cartilage increases significantly following simulated articulation and that the variability increases in post-test measurements. This stiffness increase may be attributed to fluid flow out of the explant during articulation and a compaction of the cartilage tissue, leading to a higher modulus. Over time, the explant stiffness decreases to pre-test modulus levels, indicating that stiffness increase is a transient response to articulation. Limitations include: (1) post-test indent time after articulation and its influence on mechanical properties; and (2) animal variation. Observing how mechanical properties are affected by cartilage matrix wear and identifying biochemical differences that play a role in stiffness may be of interest in future studies.
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ASSESSMENT OF THE FRACTURE RISK OF PROXIMAL PORCINE FEMURS WITH SIMULATED LESIONS USING A FRACTURE PREDICTION METHOD BASED ON BEAM THEORY

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Introduction: Current methods of diagnosing bone diseases like avascular necrosis (AVN) are subjective and no reliable assessment of the fracture risk is available. AVN leads to an interruption of the blood supply, which results in the death of bone tissue and its collapse if left untreated. A fracture prediction tool is needed to help clinicians find the most suitable treatment. One route to finding the strength of bones, including the femur, can be the utilisation of structural mechanics, where bone is a structural member subjected to load. Ohzono et al. (1991) reported that collapse of the femoral head most often occurs when the lesion location is in the weight bearing area. Therefore lesions lateral to the fovea